High-Grade Cervical Dysplasia: Pathophysiology, Diagnosis, and Treatment

Meggan Zsemlye, MD

KEYWORDS

- Cervical dysplasia • Cervical cancer
- Loop electrosurgical excision procedure
- Cold knife cone biopsy
- Human papillomavirus

PREVALENCE OF HUMAN PAPILLOMAVIRUS

Data from the 2003–2004 National Health and Nutrition Examination Survey show that the prevalence of human papillomavirus (HPV) infection in women in the United States during that time was 26.8% (95% CI, 23.3%–30.9%).[1] The prevalence was highest (44.8%) among women aged 20 to 24 (95% CI, 36.3%–55.3%) and was noted to decrease with age. Women aged 50 to 59 had a prevalence of only 19.6% (95% CI, 14.3%–26.8%). In this study the HPV types found in currently available vaccines were less common. HPV 16 was detected in 1.5% of participants (95% CI, 0.9%–2.6%), and HPV 18 was found in 0.8% (95% CI, 0.4%–1.5%) (**Box 1**).[1]As expected, independent risk factors for HPV positivity included young age, single marital status, and increased number of sexual partners.

PERSISTENCE OF HIGH-RISK HUMAN PAPILLOMAVIRUS INFECTION

Persistence of high-risk HPV infection is a key factor in the development of high-grade cervical lesions. Persistent HPV is defined as an infection lasting more than 6 to 12 months. Risk factors for persistent HPV infection include older age (>55 years), high-risk HPV type, and duration of infection.[2] The ALTS trial showed that the longer an infection is present, the longer it takes to clear. No consensus has yet been reached on the importance of measured viral load in predicting outcomes of HPV infections. Immunosuppression and cigarette smoking also are known to increase the risk for high-grade cervical disease.

Department of Obstetrics and Gynecology, University of New Mexico, MSC 10 5580 1, Albuquerque, NM 87131-5580, USA
E-mail address: mzsemlye@salud.unm.edu

Obstet Gynecol Clin N Am 35 (2008) 615–621
doi:10.1016/j.ogc.2008.09.008 **obgyn.theclinics.com**
0889-8545/08/$ – see front matter

Box 1
Commonly found human papillomavirus types

Common high-risk (oncogenic) HPV types:
16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 69, 82
Common low-risk (nononcogenic) HPV types:
6, 11, 40, 42, 43, 44, 54, 61, 72, 81

A 7-year longitudinal study from Brazil illustrates the risk for persistent HPV causing high-grade cervical dysplasia. Women in the study initially were free of dysplasia and were followed with frequent HPV testing and Papanicolaou (Pap) testing. Patients were referred for colposcopy and biopsy if their Pap test result showed high-grade squamous intraepithelial lesions (HSIL). Results showed that the relative risk for HSIL over 5 years of follow-up was 3.85 if women had been positive for HPV 16 or 18 at one visit. If they were positive for HPV 16 or 18 at two visits (showing a persistent infection), the relative risk for HSIL over the same time period was 12.27.[3]

CYTOLOGY OF HIGH-GRADE SQUAMOUS INTRAEPITHELIAL LESIONS

A Pap test result that is interpreted as HSIL includes the changes consistent with a diagnosis of cervical intraepithelial neoplasia (CIN) 2,3. These include but are not limited to hyperchromatic nuclei, abnormal chromatin distribution, nuclear pleomorphism, increased nuclear/cytoplasmic ratio, and nuclear atypia. Mild manifestations of these changes warrant a diagnosis of low-grade squamous intraepithelial lesion (LSIL) on Pap test; severe or more dramatic changes are diagnostic of HSIL. As is true in all types of cervical dysplasia, the cytologic diagnosis of HSIL is not reliably reproducible. In the ALTS trial, reviewing pathologists agreed with an initial cytologic diagnosis of HSIL only 47% of the time. This is much greater reliability/agreement than is seen with lower-grade Pap tests but still higher than is desirable.[4]

MANAGEMENT OF HIGH-GRADE SQUAMOUS INTRAEPITHELIAL LESIONS PAPANICOLAOU TEST

Guidelines for the management of abnormal Pap test results have been put forth by the American Society for Colposcopy and Cervical Pathology (ASCCP). The ASCCP held its most recent consensus conference in September 2006, at which time close to 150 experts in the fields of pathology, microbiology, and women's health and oncology gathered to review data and come up with guidelines for management of abnormal cervical cytology and histology results. Previous guidelines had been issued in 2001 but the explosion of information about HPV, its pathophysiology, and its connection with cervical dysplasia and cancer necessitated another conference in 2006. The guidelines are evidence based and freely available. Whenever the term *guidelines* is used in this article, it is in reference to the ASCCP 2006 Consensus Conference guidelines.[5]

The guidelines for the management of a Pap test result showing HSIL are straightforward. Colposcopy with endocervical assessment is acceptable as is immediate treatment with a loop electrosurgical excisional procedure in most patients.[5] The exceptions to this rule are patients who are pregnant or adolescent and have an HSIL Pap test result. The follow-up for those groups is discussed later.

Immediate loop excision of the transformation zone after an HSIL Pap test result is considered acceptable treatment because of the high likelihood that CIN 2 or worse will be found on subsequent biopsy or excision of the cervix. Women who have an